PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference R2554-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/10715	International filing date *(day/month/year)* 24.09.2003	Priority date *(day/month/year)* 30.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/00		
Applicant UNIVERSITEIT GENT et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.04.2004	17.01.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Villa Riva, A Telephone No. +49 89 2399-8404

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/10715

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-27	as originally filed

Claims, Numbers

6-18	as originally filed
1-5	received on 03.05.2004 with letter of 03.05.2004

Drawings, Sheets

1/4-4/4	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-18
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 - WO 99/63971 A , disclosing preparations with a microosmotic core, optionally coated for the controlled delivery of drugs.
D2 - WO 99/51208 A , diclosing a matrix with controlled erosion
D3 - WO 89/09066 A, disclosing preparations comprising a matrix with controlled erosion, optionally coated
D4 - US 5 213 808 A , disclosing multilayered pharmaceutical forms with a matrix and surfactant;
D5 WO 01/05376 A, disclosing felodipine pharmaceutical forms with a matrix and a "solubilizer"

Unless otherwise indicated, reference is made to the relevant passages emphasized in the International Search Report.

In several of the cited prior art items (D1, D2, D6), preparations with the same or a very similar structure structure and the same ingredients are disclosed. They also can be optionally coated. However, in all cases, the hydrophilic cellulose polymer is present in the core in a quantity which is greater than that of the amphiphilic material.
Therefore novelty is acknowledged to the present set of claims. In view of the good in vitro and in vivo results, the presence of an inventive step can be acknowledged as well.
In summary, present claims 1-18 appear to comply with the requirements of the PCT as far as novelty, inventivity and industrial applicability are concerned.

CLAIMS

1. A biologically active composite solid shaped article comprising:

(a) an outer layer comprising:

- at least one polymeric component, and
- optionally at least one plasticizer for the said polymeric component,

(b) an inner core filling the said outer layer and comprising:

- at least a biologically active ingredient, and
- an excipient for the said biologically active ingredient, said excipient comprising at least one cellulose derivative,

characterised in that the cellulose derivative of the inner core is a hydrophilic cellulose polymer, and the excipient of the inner core further comprises an amphiphilic material in the form of a blend with the said cellulose derivative, and the weight ratio of the hydrophilic cellulose polymer to the amphiphilic material in the said blend is from 0.2:1 to 0.6:1.

2. A biologically active composite solid shaped article according to claim 1, wherein the hydrophilic cellulose polymer of the inner core is a hydroxyalkylalkylcellulose.

3. A biologically active composite solid shaped article according to claim 1 or claim 2, wherein the hydrophilic cellulose polymer of the inner core is hydroxypropylmethylcellulose.

4. A biologically active composite solid shaped article according to any of claims 1 to 3, wherein the amphiphilic material of the inner core is a mixture of mono-, di- and triglycerides of polyethyleneglycol mono- and di-esters.

5. A biologically active composite solid shaped article according to any of claims 1 to 4, wherein the weight ratio of the hydrophilic cellulose polymer to the amphiphilic material in the blend of the inner core is from 0.3:1 to 0.6:1.